

REMARKS

The Office action dated September 26, 2007, is acknowledged. Claims 1-21 and 27-41 are pending in the instant application. According to the Office action, each of claims 1-21 and 27-41 has been rejected. By the present Office Action response, claims 1, 33, 34 and 41 have been amended and claims 42 and 43 have been added. Claim 1 has been amended to incorporate the recitation that the gas-forming component comprises at least one carbon dioxide-forming substance with the addition of an acid. Support for this limitation may be found in the present specification at paragraph [000053] (Examples 1 and 2), as well as in paragraphs [000013], [000014] and [000017] which have been amended herein to more accurately reflect the aforementioned limitation. It is noted that support for this limitation may also be found at page 5, last paragraph, of the original application as filed in the corresponding PCT application which states "Combined with an acid, but also without an acid ..." and in the amended page 5 of the corresponding PCT which had been amended during the international phase, which states "...carbon dioxide-forming substance without added acid ..." In this regard, it is noted that the latter phrase was inadvertently excluded from the text of the substitute specification as filed, and therefore the current amended to paragraph [000017] simply places said paragraph in agreement with amended page 5 of the corresponding PCT application. It is further noted that the English translation of the page 5 amendment erroneously translated the German term for "acid" as "salt" but that "acid" is the correct term therein. Claim 41 is amended to more precisely define the present invention. Claims 33 and 34 have been amended for clarifying antecedent basis matters. Support for new claims 42 and 43 may be found in the specification at, for example, paragraphs [000029] and [000030],

respectively. Reconsideration is respectfully requested in light of the amendments being made hereby and the arguments made herein. No new matter has been added.

Double Patenting

Claims 1-6, 8-13, 15-31 and 33-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-13, 15 and 16 of co-pending Application Serial No. 10/468,230 (U.S. Publication No. 2004/0081699) (Rademacher, et al.), in view of U.S. Publication No. 2006/0057207 (Ziegler, et al.). The Examiner states that the present claims are not patentably distinct from those of the cited references since the '230 reference recites the limitations of the present claims, except for the teaching of a carbon dioxide-forming substance. The Examiner refers to Ziegler, et al. for this missing teaching and concludes that it would be obvious to modify the teachings of Rademacher, et al. in view of Ziegler, et al. to arrive at the presently claimed invention.

Claims 1-6, 8-13, 15-31 and 33-38 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4-9, 13, 15-21, 23, 42-48 and 52-82 of co-pending Application Serial No. 10/517,093 (U.S. Publication No. 2005/0175675) (Siebertz), in view of U.S. Publication No. 2007/0122455 (Myers, et al.). The Examiner again states that the present claims are not patentably distinct from those of the cited references since the '093 reference recites the limitations of the present claims, except for the teaching of a specific water-soluble polymer. The Examiner refers to Myers, et al. for this missing teaching and concludes that it would be obvious to modify the teachings of Siebertz in view of Myers, et al. to arrive at the presently claimed invention.

The Applicants respectfully traverse the first double-patenting rejection (based on Rademacher, et al. in view of Ziegler, et al.). In particular, the present claims as amended herein are drawn exclusively to pharmaceutical preparations in which a carbon dioxide-generating substance is present without being combined with an acid component. It is submitted that this subject matter is patentably distinct from the subject matter of co-pending application Serial No. 10/468,230 (Rademacher, et al.) (as well as from co-pending Application Serial No. 10/517,093 in the name of Siebertz).

Regarding Ziegler, et al., which is cited as a secondary reference for teaching effervescent disintegration agents in the first double-patenting rejection, it is respectfully submitted that the reference should be removed from consideration. In particular, the published application is a continuation-in-part application of Application Serial No. 10/300,608, which in turn is a non-provisional patent application based on provisional application Serial No. 60/334,652 (filed on November 30, 2001). It is noted that this provisional application does not disclose effervescent disintegration agents, which were first introduced in the 10/300,608 application filed on November 20, 2002. This is a date after the February 21, 2002 priority date of the present application. In addition, the '608 application was published on September 25, 2003, which is not a date more than one year prior to the date of the application of the present application (August 20, 2004). Therefore, it is submitted that Ziegler, et al. '207 is not a proper prior art reference in view of the present application and should therefore be withdrawn from consideration.

In regards to the second double-patenting rejection (based on Seibertz in view of Myers, et al.), a properly executed terminal disclaimer is enclosed herewith.

In view of the above, withdrawal of these double-patenting rejections is respectfully requested.

Rejection of claims 33, 34 & 41 under 35 U.S.C. 112, second paragraph

Claims 33, 34 & 41 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. Claims 33, 34 and 41 have been rejected as being indefinite. In particular, the Examiner states that claims 33 and 34 recite a limitation of a “thickness” but that there is insufficient antecedent basis for this term. For example, claim 15, from which claims 33 and 34 depend, recites a “density” rather than a “thickness.” Claims 33 and 34 have been amended to change the term “thickness” to “density.” Withdrawal of this rejection is requested.

The Examiner states that the preamble of claim 41 recites “A method for administering a pharmaceutical preparation ... comprising the steps of ...” while the remainder of the claim appears to recite steps for a process for preparing a film and appears to be incomplete since the process steps may not result in a film. The Examiner has interpreted the claim to recite a method for administering a pharmaceutical preparation by applying the preparation to the surface of oral mucosa for disintegration in the aqueous media. Claim 41 has been amended accordingly, as set forth above. Withdrawal of this rejection is also requested.

Rejection of claims 1-3, 5-12, 15-21, 29-31 and 33-41 under 35 U.S.C. 102(a)

Claims 1, 2, 5-12, 16, 17, 20, 21, 29-31, 35, 36 and 39-41 have been rejected under 35 U.S.C. 102(a) as being anticipated by WO 02/02085 (corresponding to U.S. Publication No. 2004/0028732) (Falkenhausen, et al.). The Examiner essentially

concludes that Falkenhausen, et al. disclose every limitation recited in present claims 1, 2, 5-12, 16, 17, 20, 21, 29-31, 35, 36 and 39-41. In particular, the Examiner states that Falkenhausen, et al. teach a rapidly disintegrating sheet or wafer dosage form having a thickness of between 0.1-5 mm, the dosage form comprising matrix-forming polymers, active ingredients, and a carbon dioxide gas forming agent. The Examiner further states that the polymers include cellulosic polymers, and water-soluble polysaccharide. Lastly, the Examiner states that the dosage form further comprises eucalyptus oil, peppermint oil, flavor, sweetener, other additives and foams, such as propylene glycol and that the dosage form disintegrates in the oral cavity in the range from 10-30 seconds.

Claims 1-3, 5-12, 15-21, 29-31 and 33-41 are rejected as being anticipated by Ziegler, et al. As set forth on pages 6-7 of the Office action, the Examiner essentially concludes that Ziegler, et al. disclose every limitation recited in these claims. In particular, the Examiner states that Ziegler, et al. disclose a fast disintegrating film or wafer comprising an active agent, film-forming polymers, effervescent disintegrants (i.e., gas-forming agent) and filler and that film-forming polymers are disclosed in paragraph [0076] of Ziegler, et al. The Examiner also states that Ziegler, et al. teach that the film-forming polymers are added in an amount that falls within the claimed range, e.g., 0.01 – 99% and that effervescent disintegrants include sodium carbonate. Furthermore, it is stated in the Office action that the film further comprises water, additional film-forming agent, plasticizing agent, flavoring, saliva stimulating agents, cooling agent, surfactant, stabilizing agent, emulsifying agent, thickening agents, binding agent, coloring agent, sweetening agent, fragrance and the like, and that Ziegler, et al. disclose that the film has a thickness that falls within the claimed range (i.e., between 30 μ m to 300 μ m). Lastly,

the Examiner states that Ziegler, et al. disclose that the film disintegrates in a patient's oral cavity in less than one minute. The Examiner does point out that Ziegler, et al. fail to teach the claimed properties, such as the density, but that the density is inherent because Ziegler, et al. teach the use of the same polymer and the same carbon dioxide forming agent to obtain the same wafer composition having the claimed disintegrating time, and that this would be obvious to one skilled in the art.

The Applicants respectfully disagree with the Examiner's conclusion and submit that the present invention as defined in the presently amended claims 1 is patentably distinct from the inventions disclosed in both Falkenhausen, et al. and Ziegler, et al. In particular, the Applicants submit that while Falkenhausen, et al. generally teach sheet-like dosage forms that may contain carbon dioxide-forming substances, the reference fails to disclose preparations which comprise at least one carbon dioxide-forming substance which is not combined with an acid (emphasis added), as set forth in present claim 1, as amended herein.

Regarding Zeigler, et al., the provisional application which formed the basis of the Zeigler, et al. '207 reference does not teach or disclose adding effervescent disintegration agents at all. While Zeigler, et al., in the '207 application, mentions effervescent disintegrants, the reference fails to disclose any dosage form that contain carbon dioxide-forming compound that is not combined with an acid, as recited in present claim 1.

In view of the above, both Falkenhausen, et al. and Ziegler, et al. fail to teach each and every limitation of the present claims and therefore both fail to anticipate the present invention. Withdrawal of the present rejection is respectfully requested.

Rejection of claims 1--21, 27-32 and 33-41 under 35 U.S.C. 103(a)

Claims 1-12, 15-21, 27-31 and 33-41 have been rejected as being unpatentable over Ziegler, et al. in view of U.S. Publication No. 2003/0091629 (Pather, et al.). The Examiner argues that Ziegler, et al. teach every limitation of these claims (as discussed earlier) but fail to teach the claimed amount of the gas-forming agent. The Examiner notes that Ziegler, et al. do teach the use of saliva stimulating agent in an amount that falls within the claimed range (i.e., about 0.01% to about 12%) and that Ziegler, et al. disclose the use of sodium carbonate as an effervescent disintegration agent to stimulate saliva production, thereby providing additional water to aid in further effervescence and disintegration. The Examiner further argues that Pather, et al. teach an effervescing sublingual buccal dosage form comprising a drug, an additive, and an effervescent in an amount of about 5% to about 95%, as well as that the effervescent includes sodium carbonate and potassium carbonate. The Examiner concludes that it would have been obvious to one skilled in the art to modify the fast disintegrating dosage of Ziegler, et al. to include the carbonates in an amount in view of the teaching of Pather, et al. for arriving at the present invention. It is stated that this is because Pather, et al. teach the use of effervescent in an amount so as to influence the permeability of the medicament across the buccal, sublingual and gingival mucosa, because Ziegler, et al. teach the use of sodium carbonate in the dosage form, and because Ziegler, et al. teach the desirability to obtain a fast disintegrating dosage form useful for buccal and sublingual delivery.

Claims 1-12, 16, 17, 19-21, 27-31, 35, 36 and 39-41 have been rejected as being unpatentable over Falkenhausen, et al. in view of Pather, et al. As noted in the Office action on pages 9-10, the Examiner argues that Falkenhausen, et al. teach every limitation

of these claims (as discussed earlier) except for the carbon dioxide forming substance. The Examiner relies on Pather, et al. for this missing teaching of Falkenhausen, et al., in particular an effervescent sublingual buccal dosage form comprising a drug, an additive and an effervescent in an amount of about 5% to about 95%, as well as effervescent includes sodium carbonate and potassium carbonate. The Examiner thus concludes that it would have been obvious to one skilled in the art to modify the rapidly disintegrating dosage of Falkenhausen, et al. to include the carbon dioxide forming substance, such as sodium carbonate, in an amount in view of the teaching of Pather, et al. for arriving at the present invention. It is stated that this is because Pather, et al. teach the use of effervescent in an amount so as to influence the permeability of the medicament across the buccal, sublingual and gingival mucosa, because Pather, et al. teach the use of sodium carbonate to evolve gas such as carbon dioxide gas, and because Falkenhausen, et al. teach the desirability of using carbon dioxide gas forming substance.

The Examiner does note that Falkenhausen, et al. also fail to teach the amount of water-soluble polymer, but that differences in concentration will not support patentability unless there is evidence indicating such concentration is critical. Thus, it is concluded that it would have been obvious to one of ordinary skill in the art to, by routine experimentation, select an amount of matrix-forming polymer that falls within the claimed range since Falkenhausen, et al. disclose the desirability to use the same matrix-forming polymer to obtain the same film shape dosage form having the same disintegrating time.

Claim 32 has been rejected as being unpatentable over Ziegler, et al. or Falkenhausen, et al. in view of Myers, et al. As noted in the Office action on page 10, the

Examiner argues that Ziegler, et al. or Falkenhausen, et al. fail to teach ethyl cellulose as a film-forming polymer. The Examiner in turn relies on Myers, et al. for this missing teaching of Ziegler, et al. or Falkenhausen, et al. and concludes that it would have been obvious to one skilled in the art to have modified the rapidly disintegrating dosage of Ziegler, et al. or Falkenhausen, et al. using ethyl cellulose as a film-forming polymer in view of the teaching of Myers, et al. because Myers, et al. teach using ethyl cellulose in rapid-dissolve film-shaped dosage form is well known in the art and since both Ziegler, et al. or Falkenhausen, et al. teach the desirability for using cellulosic film-forming polymers.

Claims 13 and 14 have been rejected as being unpatentable over Ziegler, et al. in view of U.S. Patent No. 5,800,832 (Tapolsky, et al.). The Examiner states in the Office action that Ziegler, et al. fail to teach the film layers as claimed in claims 13 and 14. However, the Examiner relies on Tapolsky, et al. for this missing limitation and concludes that it would have been obvious to one skilled in the art to have combined the teachings of these references to arrive at the presently claimed invention as set forth in claim 32. In particular, the Examiner states that Tapolsky, et al. teach a water-soluble, bioerodable delivery device comprising an adhesive layer and a non-adhesive backing layer and that the two layers have different dissolution rate. Thus, the Examiner concludes that it would have been obvious to modify the delivery thin film of Ziegler, et al. to contain the mucoadhesive bioerodable film in view of the teaching of Tapolsky, et al. because Tapolsky, et al. teach a mucoadhesive bioerodable film provides adhesive to mucosal surface with minimal discomfort and ease of use, because Tapolsky, et al. teach

using mucoadhesive to maintain the delivery device at the site of treatment, and because Ziegler, et al. teach the thin film delivery system includes multi-layer system.

The Applicants respectfully submit that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitation. The Applicants respectfully submit that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider the teachings of the cited prior art alone, or in combination, each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success if the aforementioned references were to be considered. In addition, prior art must be considered in its entirety, i.e., as a whole (emphasis provided), including portions that would lead away from the claimed invention (M.P.E.P. §2141.02, citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220, USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)), proposed modification cannot render the prior art unsatisfactory for its intended purpose or change the principle of operation of a reference (M.P.E.P. §2143.01), and Examiner's conclusion of obviousness may not be based on improper hindsight (M.P.E.P. §2145(X)(A)).

The Applicants first submit that the present invention is based on the unexpected finding that the unpleasant sensation caused by bitter-tasting substances present in a pharmaceutical preparation can be abolished, or at least strongly reduced, by adding

carbon dioxide-forming compounds. To achieve such a “taste-masking” effect, it is not necessary to combine the carbon dioxide-forming compound with an acidic component, as demonstrated by Examples 1 and 2 of the instant specification. In contrast, according to the cited prior art, carbon dioxide-forming compounds are used as effervescent and admixture of an acidic component is generally regarded as being necessary as a reaction partner in the chemical reaction which generates carbon dioxide. It is therefore apparent that the cited prior art references teach away from the presently claimed invention, as explained further below.

The Applicants first respectfully disagree with the Examiner’s opinions for at least the reasons set forth above regarding Ziegler, et al., in particular since Ziegler, et al. should be withdrawn from consideration as prior art. In addition, it is respectfully submitted that Zeigler, et al. ‘207 only teach that effervescent disintegration could be brought about by combining a soluble acid source and an alkali metal carbonate (paragraph [0048]). Similarly, Pather, et al. teach that production of gas is the result of the chemical reaction of a soluble acid source and a source of carbon dioxide (paragraph [0015]). It is submitted that this teaching differs from the presently claimed invention in that the present invention provides that a carbon dioxide-forming agent is present which is not combined with an acid. Moreover, it is submitted that neither Zeigler, et al. or Pather, et al. teach or otherwise suggest a taste-masking effect that may be caused by incorporating carbon dioxide-forming substances.

Turning now to Falkenhausen, et al., it is respectfully submitted that the reference mentions gas-forming excipients (paragraph [0036]) which, according to Pather, et al., comprise a soluble acid source and a source of carbon dioxide which two components

take part in a chemical reaction which produces the gas (paragraph [0015]). It is submitted that this teaching is distinct from the presently claimed invention in that the present invention does not rely on the combined presence of an acid and a carbon dioxide-forming substance – again, therefore teaching away from the presently claimed invention. Therefore, it is respectfully submitted that this rejection be withdrawn.

Regarding the rejection of claim 32 as being unpatentable over Ziegler, et al. or Falkenhausen, et al. in view of Myers, et al., the Applicants respectfully traverse for at least the numerous deficiencies of Ziegler, et al. or Falkenhausen, et al., discussed above. Moreover, Myers, et al. was cited merely for teaching ethyl cellulose as a film-forming polymer and fails to make up for the aforementioned deficiencies of Ziegler, et al. or Falkenhausen, et al. Therefore, it is respectfully submitted that this rejection be withdrawn.

Regarding the rejection of claims 13-14 as being unpatentable over Ziegler, et al. in view of Tapolsky, et al., the Applicants respectfully traverse for at least the various deficiencies of Ziegler, et al., discussed above. Moreover, Tapolsky, et al. was cited merely for teaching a bilayer comprising a non-mucoadhesive layer and fails to make up for the deficiencies of Ziegler, et al. Therefore, it is respectfully submitted that this rejection be withdrawn.

It is therefore respectfully submitted that the present invention defined in the presently amended claims is patentably distinguishable over the combination of prior art teachings under 35 U.S.C. 103(a). Based on the aforementioned differences, each and every element of the present invention recited in the instant claims are not taught or disclosed in the prior art references, alone or in combination. Moreover, one skilled in

the art would not be motivated to combine the teachings of said references or to modify the cited prior art references to arrive at the presently claimed invention, and the cited prior art references teach away from the present invention. Therefore, the Applicants respectfully request that these obviousness rejections be withdrawn.


Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art references, the Applicants strongly urge that the obviousness-type rejection and anticipation rejections be withdrawn. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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